

The diagram illustrates the integrated regulation of the renal collecting duct. The duct is represented as a horizontal bar with various receptors and channels.

- Angiotensin Receptor (ATIR):** Activated by ANG I, leading to vasoconstricting, growth promoting, and aldosterone activating effects.
- Angiotensin Converting Enzyme (ACE):** Located above the duct, converting ANG I to ANG II.
- K⁺ Channel:** Facilitates K⁺ secretion, which is stimulated by cGMP-PK.
- NO (Nitric Oxide):** Released from the duct, stimulated by BK (Bradykinin).
- cGMP:** A central signaling molecule that inhibits the K⁺ channel and is produced by GC (guanylate cyclase) activated by NO and by R_s (sodium guanylate cyclase) activated by ANP+BNP and CNP.
- Guanylate Cyclase (GC):** Enzymes located on the duct membrane that produce cGMP from their respective ligands.
- Natriuretic Peptide Receptors (R_A, R_B):** Activated by ANP+BNP and CNP, leading to the production of cGMP.
- NEP 24.11 (Natriuretic Peptide Degrading Enzyme):** Degrades ANP+BNP and CNP.
- cGMP-PK:** Activated by cGMP, leading to K⁺ secretion and inhibition of the K⁺ channel.
- PDE (Phosphodiesterase):** Degrades cGMP.
- Overall Effects:** The integrated signaling leads to natriuretic, renin and aldosterone inhibiting, vasorelaxing, anti-fibrotic, and lusitropic effects.

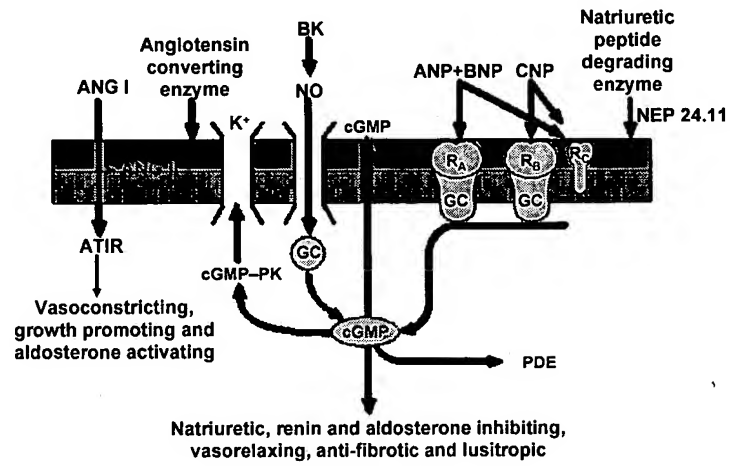
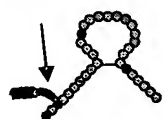


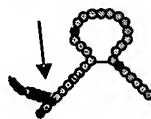
Figure 2:

Class 1: Nonhydrolyzable— conjugated drug remains intact

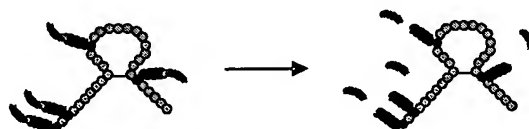
Alkyl inside



PEG inside



Class 2: Micropegylated— alkyl portion cleaved *in vivo*



Class 3: Fully hydrolyzable— entire oligomer cleaved *in vivo*

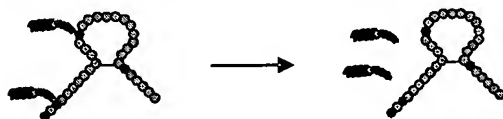


Figure 3:

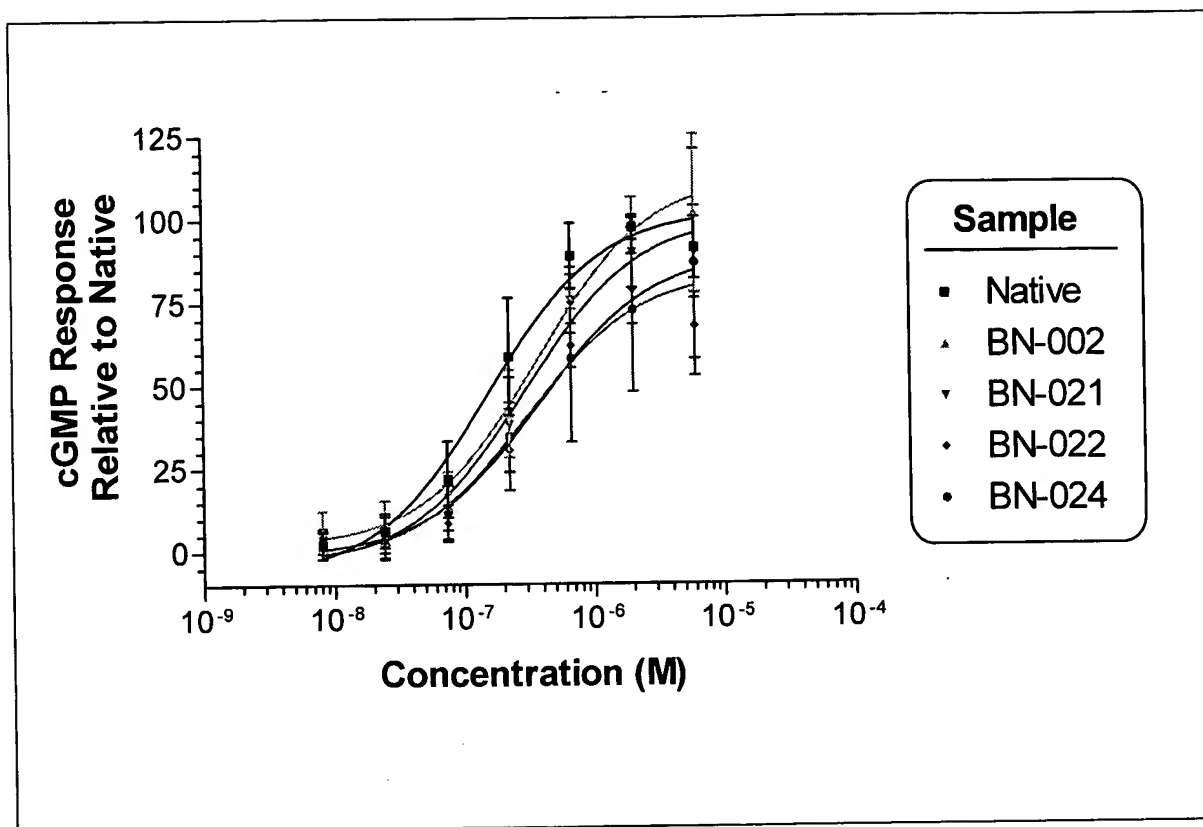


Figure 4:

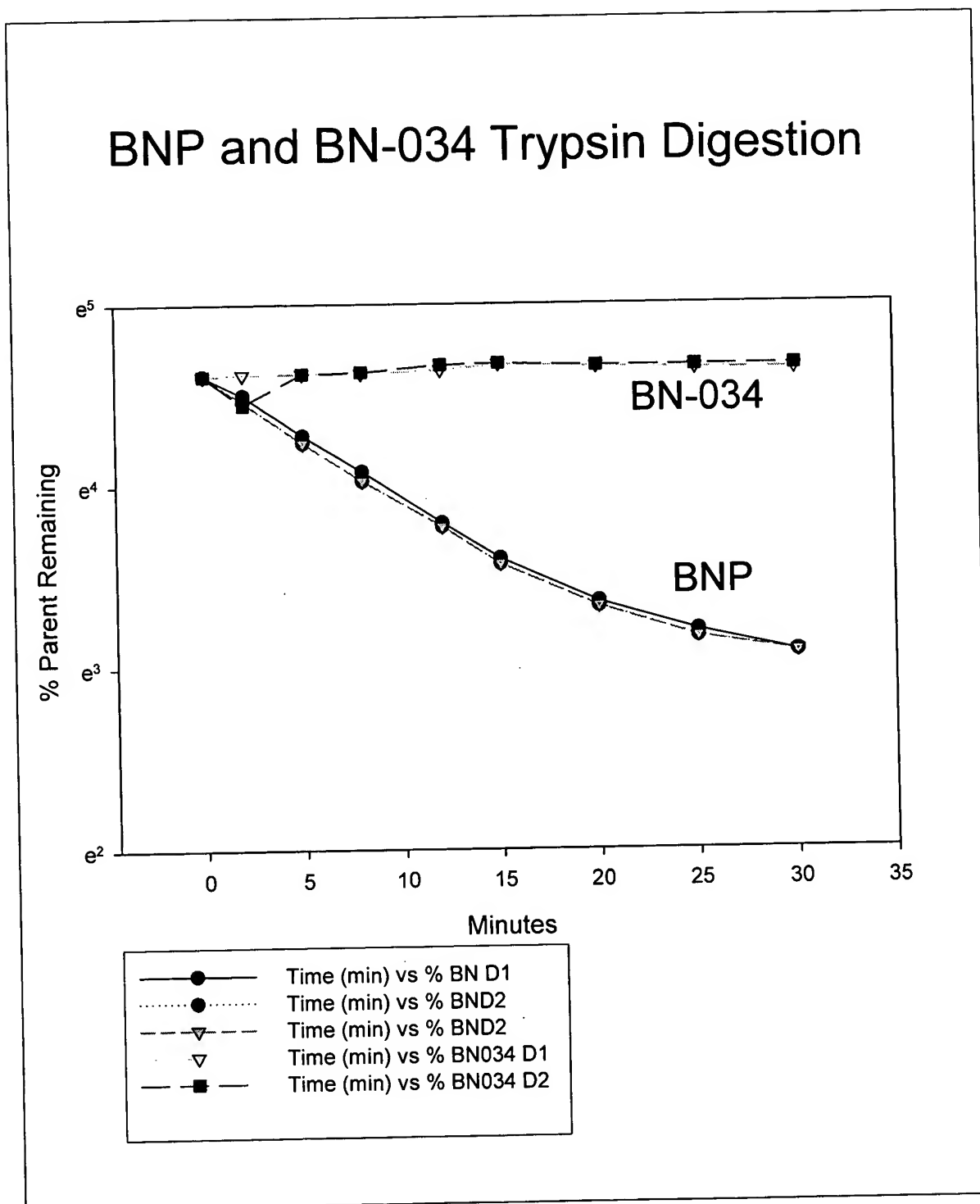


Figure 5:

Figure 5: Plasma levels of hBNP conjugates at various times after oral dosing.

